K120267

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510(k) Summary

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Idaho Technology Inc.

Modification of
FilmArray® Respiratory Panel (RP)
to add assays for Coronavirus OC43, Coronavirus 229E, *Bordetella pertussis*, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

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Device Name and Classification:

Trade Name: **FilmArray® Respiratory Panel (RP)**

Regulation Number: 21 CFR 866.3980, 21 CFR 866.3065, 21 CFR 866.3375, and 21 CFR.3120

Classification Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay, *Bordetella* spp. serologic reagents, *Mycoplasma* spp. serologic reagents, and *Chlamydia* serological reagents

Predicate Device:

K 103175 and K110764 - FilmArray Respiratory Panel (RP) System

Intended Use:

- FilmArray Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with the FilmArray instrument for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Rhinovirus/Enterovirus, Respiratory Syncytial Virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the Film Array RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

  Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Bordetella pertussis*, Coronavirus 229E, Coronavirus OC43, Influenza A/H1, Influenza A/H3, Influenza A/2009 H1, Influenza B, *Mycoplasma pneumoniae* Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for *Chlamydophila pneumoniae* were established primarily using contrived clinical specimens.

  Due to the genetic similarity between human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

  The FilmArray RP detects Adenovirus species C serotype 2 and serotype 6 with reduced sensitivity. It is recommended that specimens found to be negative for Adenovirus after examination using FilmArray RP be confirmed by an alternate method (e.g., FDA cleared molecular test or cell culture).

  The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for influenza A were established when influenza A/2009 H1N1, A/H1, and A/H3 were the predominant influenza A viruses in circulation. Performance of detecting influenza A may vary if other influenza A strains are circulating or a novel influenza A virus emerges. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Device Description:

The FilmArray RP System is a multiplex nucleic acid test system composed of the FilmArray instrument, the FilmArray software (preinstalled on a laptop computer) and the FilmArray RP pouch. The FilmArray RP pouch contains freeze-dried reagents to perform nucleic acid purification, reverse transcription, and nested, multiplex PCR with DNA melt analysis. The Respiratory Panel (RP) pouch identifies 20 common and emerging viral respiratory pathogens (see Table 1).

Table 1. Organisms Detected by the FilmArray Respiratory Panel

Viral Respiratory Pathogens
Influenza A
H1 subtype
H3 subtype
2009 H1 subtype
Influenza B
Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
Human Metapneumovirus
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus
Rhinovirus and Enterovirus
Bacterial Respiratory Pathogens
Bordetella pertussis
Chlamydophila pneumoniae
Mycoplasma pneumoniae

A test is initiated by loading Hydration Solution and an unprocessed patient nasopharyngeal swab (NPS) specimen (i.e., specimen mixed with Sample Buffer) into the FilmArray RP pouch. The pouch contains all of the reagents required for specimen testing and analysis in a freeze-dried format; the addition of Hydration Solution and specimen/Sample Buffer Mix rehydrates the reagents. After the pouch is prepared, the

FilmArray software guides the user though the steps of placing the pouch into the instrument, scanning the pouch barcode, entering the sample identification, and initiating the run.

The FilmArray instrument contains a coordinated system of inflatable bladders and seal points, which act on the pouch to control the movement of liquid between the pouch blisters. When a bladder is inflated over a reagent blister, it forces liquid from the blister into connecting channels. Alternatively, when a seal is placed over a connecting channel it acts as a valve to open or close a channel. In addition, electronically controlled pneumatic pistons are positioned over multiple plungers in order to deliver the rehydrated reagents into the blisters at the appropriate times. Two Peltier devices control heating and cooling of the pouch to drive the reverse transcription reactions, the PCR reactions, and the melting curve analysis.

Nucleic acid extraction occurs within the FilmArray pouch using mechanical lysis and standard magnetic bead technology. After extracting and purifying nucleic acids from the unprocessed sample, the FilmArray performs a nested multiplex PCR that is executed in two stages. During the first stage, the FilmArray performs a single, large volume, highly multiplexed reverse transcription PCR (rt-PCR) reaction. The products from first stage PCR are then diluted and combined with a fresh, primer-free master mix and a fluorescent double stranded DNA binding dye (LC Green®Plus, Idaho Technology). This second master mix solution, is then distributed to each well of the array. Array wells contain sets of primers designed specifically to amplify sequences internal to the PCR products generated during the first stage PCR reaction. The second stage PCR, or nested PCR, is performed in singleplex fashion in each well of the array. At the conclusion of the 2nd stage PCR, the array is interrogated by melting curve analysis for the detection of signature amplicons denoting the presence of specific viral or bacterial targets. A digital camera placed in front of the second stage PCR captures fluorescent images of the PCR reactions in real time.

The FilmArray software automatically interprets the results of each DNA melting curve analysis and combines the data with the results of the internal pouch controls to provide a test result for each organism on the panel.

Substantial Equivalence:

The FilmArray Respiratory Panel System is substantially equivalent to the FilmArray Respiratory Panel System K103175 (cleared on February 17, 2011) and K110764 (cleared on April 27, 2011). Both were determined to be class II devices.

The following tables compare the FilmArray RP to the previously cleared FilmArray RP (K103175 and K110764). The first table outlines the similarities between the two systems and the following table outlines the differences.

Similarities between the New Device and the Predicate.

Element	New Device: FilmArray Respiratory Panel System	Predicate: FilmArray Respiratory Panel System (K103175 and K110764)
Analyte	RNA/DNA	Same
Technological Principles	Multiplex nucleic acid	Same
Specimen Types	Nasopharyngeal swabs	Same
Technological Principles	Nested multiplex RT-PCR followed by high resolution melting analysis to confirm identity of amplified product.	Same
Instrumentation	FilmArray Instrument	Same
Time to result	Less than 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Sample Preparation Method	Sample Processing is automated in the FilmArray instrument.	Same
Reagent Storage	Reagents are stored at room temperature.	Same
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis.	Same
User Complexity	Moderate/Low	Same

Differences between the New Device and the Predicate.

Element	New Device: FilmArray Respiratory Panel System	Predicate: FilmArray Respiratory Panel System (K103175 and K110764)
Organisms Detected	Same as predicate with additional organisms: *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Bordetella pertussis,* Coronavirus 229E, and Coronavirus OC43.	Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Respiratory Syncytial Virus, Human Metapneumovirus, Adenovirus, Parainfluenza 1, Parainfluenza 2, Parainfluenza virus 3,Parainfluenza 4, Rhinovirus/Enterovirus, Coronavirus HKU1 and Coronavirus NL63.

Summary of Performance Data for Coronavirus 229E, Coronavirus OC43, *Bordetella pertussis, Chlamydophila pneumoniae,* and *Mycoplasma pneumoniae*

Clinical Performance

The clinical performance of the FilmArray RP system for Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* was established during a prospective study at 3 U.S. clinical sites where enrollment spanned an 11 month time period encompassing two respiratory seasons (December 2009 - May 2010 and September 2010 – January 2011). Subjects with signs and/or symptoms of respiratory infection were invited to participate. Upon obtaining informed consent, NPS samples were collected for FilmArray and comparator testing; a second respiratory sample was collected from each subject for viral culture reference testing. A total of 1144 subjects were initially enrolled in the study (857 between December 2009 and May 2010; 287 between September 2010 and January 2011) and four were withdrawn. Specimens from 20 subjects were omitted from analysis due to improper storage prior to testing, and three specimens were omitted due to external control failures on the day of testing. Table 2 provides a summary of demographic information for the remaining 1117 subjects that participated in the prospective study.

Table 2. Demographic Summary for FilmArray RP Prospective Study

Sex	**Number of Subjects**
Male	600 (54%)
Female	517 (46%)
Age	
≤5	719 (64%)
6-21	124 (11%)
22-49	190 (17%)
≥50	84 (8%)

Each NPS specimen was tested with the FilmArray RP. The performance of the FilmArray RP for Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* was evaluated by comparing the FilmArray RP test result for each virus or bacteria with the appropriate comparator/reference methods shown in Table 3.

Table 3. Reference/Comparator Methods Used to Assess FilmArray RP performance

Organism/Virus	Reference/Comparator Method(s)
Coronavirus 229E	**2 PCR tests of patient specimen with bi-directional sequence confirmation[1]**
Coronavirus OC43	
Bordetella pertussis	
Chlamydophila pneumoniae	
Mycoplasma pneumoniae	

[1] Performance of the FilmArray RP system detecting Coronavirus 229E, Coronavirus OC43, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*, respectively, was compared to a predetermined algorithm that used composite comparator methods. The methods consist of two analytically validated PCR assays followed by bi-directional sequencing. The comparator assays were designed to amplify a different sequence from that amplified by the FilmArray assay(s). None of the comparator PCR assays overlapped any FilmArray amplicon sequence even if the same gene was targeted. "True" positives were considered as any sample that had bi-directional sequencing data meeting pre-defined quality acceptance criteria that matched sequences deposited in the National Center for Biotechnology Information (NCBI) GenBank database (www.ncbi.nlm.nih.gov) with acceptable E-values. "True" negatives were considered as any sample that tested negative by both of the comparator PCR assays.

A total of 1117 specimens were evaluated for Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* in this study. Clinical sensitivity or positive percent agreement (PPA) was calculated as 100% x (TP / TP + FN). True positive (TP) indicates that both the FilmArray RP and comparator method had a positive result for this specific analyte and false negative (FN) indicates that the FilmArray result was negative while the comparator result was positive. Specificity or negative percent agreement (NPA) was calculated as 100% x (TN / TN + FP). True negative (TN) indicates that both the FilmArray RP and the comparator method had negative results and a false positive (FP) indicates that the FilmArray RP result was positive but the comparator results was negative. The exact binomial two-sided 95% confidence interval was calculated. The results are summarized in Table 4.

Table 4. Clinical Sensitivity and Specificity for the FilmArray RP Prospective Clinical Study

Analyte	Positive Percent Agreement			Negative Percent Agreement		
	TP/ TP + FN	Percent	95% CI	TN/ TN + FP[a]	Percent	95% CI
Coronavirus 229E	12/12	100%	73.5-100%	1103/1105[a]	99.8%	99.4-100%
Coronavirus OC43	14/14	100%	76.8-100%	1098/1103[b,c]	99.6%	99.0-99.9%
B. pertussis	6/6	100%	54.1-100%	1110/1111	99.9%	99.5-100%
C. pneumoniae	1/1	100%	n/a	1116/1116	100%	99.7-100%
M. pneumoniae	4/4	100%	39.8-100%	1113/1113	100%	99.7-100%

a. CoV-229E was identified by bi-directional sequence analysis in 1/2 false positive specimens using an alternate assay.
b. CoV-OC43 was detected in 2/5 false positive specimens using an alternate assay with bi-directional sequence analysis.
c. 2/5 false positives were determined to be cross-reactive products derived from amplification of CoV-HKU1 virus nucleic acid with the CoV-OC43 assay primers.

A total of 121 co-infections (10.8% of all analyzed specimens; 121/1117) were detected by FilmArray during this study. The FilmArray detected 21 co-infections involving Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* (Table 5), representing approximately 17.4% of all co-infections detected (21/121).

Table 5. Co-infections Involving CoVs OC43, CoV 229E, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* as Detected by FilmArray RP

Distinct Co-infection Combinations Detected by FilmArray RP				Total Co-infections	Number of Discrepant Co-infections[a]	Discrepant Analyte(s)[a]
Analyte 1	Analyte 2	Analyte 3	Analyte 4			
CoV OC43	HRV/Entero[b]	-	-	5	0	
CoV OC43	RSV	-	-	3	3	CoV OC43 (2)[c], RSV (2)[c]
CoV OC43	CoV HKU1	-	-	2	2	CoV OC43[c,d]
CoV OC43	Adenovirus	-	-	1	0	
CoV OC43	hMPV	-	-	1	0	
CoV 229E	Adenovirus	RSV	-	1	1	Adeno[c], RSV[c]
CoV 229E	CoV NL63	HRV/Entero	RSV	1	1	CoV 229E[c], RSV[c]
CoV 229E	HRV/Entero	-	-	1	0	
CoV 229E	RSV	-	-	1	0	
B. pertussis	HRV/Entero[b]	-	-	2	1	HRV/Entero
B. pertussis	Adenovirus	HRV/Entero	-	1	1	Adeno[c], *B. pertussis*[c]
C. pneumoniae	Adenovirus	-	-	1	0	
M. pneumoniae	PIV 2	-	-	1	0	
Total Co-infections21					**Total Analytes in 21 Co-infections = 46 Discrepant Analytes = 12/46**	

a. A discrepant co-infection or discrepant analyte was defined as one that was detected by FilmArray RP but not detected by the reference/comparator methods.

b. HRV/Entero was not analyzed by a comparator method for 1/2 of the *B. pertussis* + HRV/Entero, or any of the HRV/Entero CoV OC43 co-infections due to the HRV/Entero analyte being cleared (k103175) prior to testing of these specimens.

c. These 11 discrepant analytes were investigated using bi-directional sequence analysis; 6/11 analytes were detected. Those not detected included 1 Adenovirus and 1 *B. pertussis* (Adeno/*B. pertussis*/HRV-Entero infection), 1 RSV (1 COV-OC43/RSV infection) and 2 CoV-OC43 (2 CoV-HKU1/CoV-OC43 infections).

d. Both discrepant CoVOC43 results were false-positive due to cross-reactivity of the OC43 assay with HKU1 viruses in the specimens. Users will be notified of the possibility of cross-reactivity when both of these CoVs are reported as detected in the same specimen.

Table 6 provides a summary of the FilmArray RP test results for Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* obtained during this study, including the prevalence of each organism detected by the FilmArray RP System and distribution among the age groups. The majority of Coronavirus 229E, Coronavirus OC43, *B. pertussis, C. pneumoniae,* and *M. pneumoniae* organisms were detected in children five years and younger (60%; 27/45). Of the remaining organisms 11% (5/45) were detected in subjects 6-21 years of age, 20% (9/45) in subjects 22-49 years of age, and 9% (4/45) in subjects ≥ 50 years of age.

Table 6. Prevalence and Age Distribution of Analytes in the Clinical Study

Analyte	Total (Expected Value)	≤ 5 years	6-21 years	22-49 years	≥ 50 years
Coronavirus 229E	14 (1.2%)	6	2	5	1
Coronavirus OC43	19 (1.7%)	13	2	2	2
B. pertussis	7 (0.6%)	5	1	0	1
C. pneumoniae	1 (0.09%)	1	0	0	0
M. pneumoniae	4 (0.4%)	2	0	2	0

All five organisms were of low prevalence during the clinical study (0.09 – 1.7%). To supplement the results of the prospective clinical study, an evaluation of preselected archived samples was performed.

Testing of Preselected Archived Specimens

In addition to the prospective clinical study, archived clinical NPS specimens were also tested using the FilmArray RP. The specimens were selected because they had previously tested positive for *B. pertussis*, Coronavirus 229E, Coronavirus OC43, or *M. pneumoniae*. The analyte content of each specimen was confirmed using analyte-specific PCR and bi-directional sequencing; the results of confirmation testing (positive or negative for a particular analyte) were used for the final analysis regardless of the previous laboratory test result.

The specimens were organized into "test panels" and randomized such that the users testing the samples with the FilmArray RP were blinded as to the expected test result. Each panel contained specimens known to be positive and negative for the specific analyte being evaluated allowing the calculation of a positive percent agreement (PPA) and a negative percent agreement (NPA). A summary of the available demographic information of the tested samples is provided in Table 7, and Table 8 shows the performance data summary for *B. pertussis*, Coronavirus 229E, Coronavirus OC43, and *M. pneumoniae*, and the results of confirmation testing for each analyte are detailed in the footnotes of Table 8.

Table 7. Demographic Summary of FilmArray RP Archived Specimen Study

Total Specimens		305
Sex	Female (%)	126 (41.3%)
	Male (%)	131 (43%)
	Unknown[a]	48 (15.7%)
Age	Avg	13
	Median	7
	Min	0.5

	Max	91
Age Range	≤5	141 (53%)
	6-21	76 (28.6%)
	22-49	19 (7.1%)
	≥50	27 (10.2%)
	≥5[b]	3 (1.1%)
	Unknown[a]	39 (12.8%)

[a] Demographic information was not provided for specimens from one source. Because the specimens were provided by a pediatric hospital, it is understood that the age range of specimens was from <1 yrs to 21 yrs.
[b] One source provided age category "less than 5 years of age or equal to/greater than 5 years of age"

Table 8. FilmArray Archived Specimen Performance Data Summary for *B. pertussis*, Coronavirus 229E, Coronavirus OC43, and *M. pneumoniae*.

	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	TP/TP +FN	Percent	95% CI	TN/TN+FP	Percent	95% CI
B. pertussis	53/56[a]	94.6%	85.1-98.9%	56/58[b]	96.5%	88.1-99.6%
Coronavirus 229E	13/13	100%	75.3-100%	45/47[c]	95.7%	85.5-99.5%
Coronavirus OC43	24/24	100%	85.8-100%	33/36[d]	91.7%	77.5-98.2%
M. pneumoniae	54/64[e]	84.4%	73.1-92.2%	58/56[f]	89.2%	79.1-95.6%

[a] Two (2) *B. pertussis*-positive specimens were originally identified by the source lab as negative for *B. pertussis* but were unexpectedly found to be positive by analyte specific PCR followed by bidirectional sequencing. Both of these specimens were negative when tested with the FilmArray, and both were found to be negative for *B. pertussis* during discrepancy investigation of confirmation testing.
[b] Ten (10) *B. pertussis*-negative specimens were originally identified by the source lab as positive for *B. pertussis* but this could not be confirmed by analyte specific PCR followed by bidirectional sequencing. Two (2) of these specimens were positive when tested with the FilmArray and both of these specimens were found to be positive for *B. pertussis* during discrepancy investigation of confirmation testing. Two (2) source laboratory positive samples were found to contain *B. holmesii*, both of these samples gave the expected negative result when tested with the FilmArray RP.
[c] One (1) CoV 229E-negative specimen was originally identified by the source lab as positive for CoV 229E but this could not be confirmed by analyte specific PCR followed by bidirectional sequencing. This specimen was positive when tested with the FilmArray RP.
[d] Four (4) CoV OC43-negative specimen were originally identified by the source lab as positive for CoV OC43 but this could not be confirmed by analyte specific PCR followed by bidirectional sequencing. Two (2) of these specimens were positive when tested with the FilmArray RP.
[e] The Ct results obtained during confirmation PCR testing for the 10 samples that were not detected by FilmArray indicated low analyte levels in the sample (Ct range 34.3-38.7) possible resulting from sample degradation during storage of these archived specimens.
[f] Twenty-two (22) *M. pneumoniae*-negative specimens were originally identified by the source lab as positive for *M. pneumoniae* but this could not be confirmed by analyte specific PCR followed by bidirectional sequencing. Seven (7) of these specimens were positive when tested with the FilmArray RP.

Testing of Contrived *C. pneumoniae* Specimens

Archived nasopharyngeal swab specimens that have previously tested positive for *C. pneumoniae* were unavailable for testing. Therefore, contrived *C. pneumoniae* specimens were used as surrogate clinical specimens to test the sensitivity and specificity of the

FilmArray RP *C. pneumoniae* assay. Residual specimens that had been collected during the prospective clinical evaluation were spiked with *C. pneumoniae* at clinically relevant levels (or unspiked; 50 of each). The analyte status of each contrived specimen was blinded to the users analyzing the specimens. Results of FilmArray testing are presented in Table 9.

Table 9. FilmArray Performance Data Summary for contrived *C. pneumoniae* specimens.

	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	TP/TP +FN	Percent	95% CI	TN/TN+FP	Percent	95% CI
C. pneumoniae	50/50	100%	92.9 – 100%	50/50	100%	92.9 – 100%

Selected Analytic Studies

Limit of Detection

The analytical sensitivity or Limit of Detection (LoD) for each FilmArray RP analyte was determined by testing limiting dilutions of quantified cultures of virus or bacterium. LoD is defined as the lowest concentration at which the analyte is consistently detected (detection in ≥95% of samples tested). Simulated NPS sample matrix (cultured human cells in VTM) was spiked with one or more analytes and at least 20 replicates were tested at the LoD concentration. The LoD concentrations for the FilmArray RP analytes CoV OC43, CoV 229E, *B. pertussis*, *C. pneumoniae*, and *M. pneumoniae* are listed in Table 10.

Table 10. LoD for Analytes Detected by FilmArray RP

Organism	Strain	LoD Concentration
CoV OC43	ATCC VR-759	600 $TCID_{50}$/mL
CoV 229E	ATCC VR-740	4 $TCID_{50}$/mL
B. pertussis	A639	4000 CFU/mL
C. pneumoniae	TW183	3000 DNA copies/mL
M. pneumoniae	M129 (Type 1)	30 $TCID_{50}$/mL

NOTE: CoV OC43, CoV 229E and *M. pneumoniae* were grown and quantified in $TCID_{50}$ (50% Tissue Culture Infectious Dose). The unit $TCID_{50}$ is a measure of infectivity or cytotoxicity rather than number of organisms or copies of nucleic acid. Variability in $TCID_{50}$/mL may not accurately reflect differences in the relative sensitivity of detection between different organisms or different strains of the same organism.

Analytical Reactivity (Inclusivity)

The analytical reactivity of the FilmArray RP system assays was evaluated with an inclusivity panel consisting of strains or isolates that represent the genetic, temporal, and geographic diversity of the FilmArray RP analytes. The tested organisms include: 2 Coronavirus (1 229E and 1 OC43), 9 *B. pertussis*, 4 *C. pneumoniae*, and 9 *M. pneumoniae*. Each strain was initially tested in a simulated NPS sample matrix at or near the system LoD. Higher concentrations were tested if the analyte was not detected at LoD.

Results from inclusivity testing of CoV OC43, CoV 229E, *B. pertussis*, *C. pneumoniae*, and *M. pneumoniae* are presented in Table 11. The concentration and multiple of LoD at which each strain was detected by the FilmArray RP system is indicated.

Table 11. Results of Inclusivity Testing

Organism	Strain / Isolate	Concentration Detected	Multiple of LoD Detected
CoV OC43	ATCC VR-759	600 $TCID_{50}$/mL	1x
CoV 229E	ATCC VR-740	4 $TCID_{50}$/mL	1x
B. pertussis	A639	4000 CFU/mL	1x
	E341	4000 CFU/mL	1x
	F (ATCC 8467)	4000 CFU/mL	1x
	5 [17921] (ATCC 9340)	4000 CFU/mL	1x
	18323 [NCTC 10739] (ATCC 9797)	4000 CFU/mL	1x
	10-536 (ATCC 10380)	4000 CFU/mL	1x
	CNCTC Hp 12/63 [623] (ATCC 51445)	4000 CFU/mL	1x
	Tohama I (ATCC BAA-589) (vaccine strain)	4000 CFU/mL	1x
	MN2531 (ATCC BAA-1335)	4000 CFU/mL	1x
C. pneumoniae	AR-39 (ATCC 53592)	3000 copies/mL	1x
	CDC/CWL-029 (VR-1310)	3000 copies/mL	1x
	CM-1 (ATCC VR-1360)	3000 copies/mL	1x
	TW183 (ATCC VR-2282)	3000 copies/mL	1x
M. pneumoniae	M129 (Type 1)	30 $TCID_{50}$/mL	1x
	M129-B7 (ATCC 29342) (Type 1)	300 CCU/mL [a]	10x [b]
	PI 1428 (ATCC 29085) (Type 1)	3,000 CCU/mL [a]	100x [b]
	FH strain [NCTC 10119] (ATCC 15531) (Type 2)	300 CFU/mL [c]	n/a [c]
	[Mac] (ATCC 15492) (Type 2)	300 CCU/mL [a]	10x [b]
	[M52] (ATCC 15293)	300 CCU/mL [a]	10x [b]
	[Bru] (ATCC 15377)	30,000 CCU/mL [a]	1,000x [b]
	Mutant 22 (ATCC 39505)	30 CCU/mL [a]	1x [b]
	UMTB-10G (ATCC 49894)	300 CCU/mL [a]	10x [b]

[a] CCU = Color Changing Unit. Both $TCID_{50}$ and CCU were determined according to the Reed-Muench method. Quantification in CCU/mL was considered equivalent to quantification in $TCID_{50}$/mL.

[b] Following inclusivity testing, all *M. pneumoniae* isolates previously quantified in CCU/mL were re-evaluated by real-time PCR against a standard curve of the LoD strain (M129, $TCID_{50}$/mL). Based on relative molecular quantification, all isolates were detected at levels <1x – 10x LoD, rather than 1-1,000x LoD determined by CCU/mL. ATCC 49894, ATCC 15293, ATCC 29342, and ATCC 39505 were detected at or below 1x LoD, while ATCC 15492, ATCC 29085, and ATCC 15377 were detected between 1-10x LoD.

[c] This was the only *M. pneumoniae* isolate in the panel able to form colonies on plates and was quantified in CFU/mL (Colony Forming Units).

Analytical Specificity (Cross-reactivity and Exclusivity)

The potential for cross-reactivity between assays contained in the FilmArray RP system was evaluated by testing simulated NPS samples containing high concentrations of respiratory

panel viruses and bacteria (tens to thousands-fold higher than LoD). No cross-reactivity was observed at the concentrations listed in Table 12.

Table 12. Results of Testing for Cross-Reactivity with FilmArray RP Analytes

Virus or Bacterium	Type / Strain	Test Concentration	Multiple of LoD
Adenovirus	**Serotype 1** (Species C)	$1.00x10^5$ $TCID_{50}$/mL	333x
Coronavirus	**229E** ATCC VR-740	$5.67x10^3$ $TCID_{50}$/mL	1,418x
	HKU1 – Type B Clinical specimen	$2.78x10^9$ copies/mL	1,463x
	NL63 NR-470	$5.67x10^3$ $TCID_{50}$/mL	1,134x
	OC43 ATCC VR-759	$7.30x10^4$ $TCID_{50}$/mL	122x
Human Metapneumovirus	**Type A1 - hMPV-16** IA10-2003 A1	$8.17x10^3$ $TCID_{50}$/mL	4,085x
Human Rhinovirus / Enterovirus	**Echovirus 6**	$3.40x10^6$ $TCID_{50}$/mL	113x
	Rhinovirus A1	$5.67x10^3$ $TCID_{50}$/mL	5,670x
Influenza A H1N1	**A/Brisbane/59/07**	$1.00x10^5$ $TCID_{50}$/mL	500x
	A/New Caledonia/20/99	$1.00x10^5$ $TCID_{50}$/mL	500x
	A/PR/8/34	$1.00x10^6$ $TCID_{50}$/mL	5,000x
	A1/FM/1/47	$4.70x10^3$ $TCID_{50}$/mL	24x
	A/NWS/33	$4.70x10^3$ $TCID_{50}$/mL	24x
	A1/Denver/1/57	$4.70x10^3$ $TCID_{50}$/mL	24x
	A/Solomon Islands/3/2006	$1.39x10^4$ $TCID_{50}$/mL	70x
	A/Weiss/43	$4.70x10^3$ $TCID_{50}$/mL	24x
	A/Mal/302/54	$1.39x10^4$ $TCID_{50}$/mL	70x
Influenza A H1N1-2009	**A/SwineNY/03/2009**	$4.00x10^5$ $TCID_{50}$/mL	4,000x
Influenza A H3N2	**A/Wisconsin/67/2005**	$8.17x10^3$ $TCID_{50}$/mL	1634x
	A/Victoria/3/75	$4.70x10^3$ $TCID_{50}$/mL	940x
	A/Port Chalmers/1/73	$5.67x10^3$ $TCID_{50}$/mL	1,134x
	A/Aichi/2/68	$1.00x10^5$ $TCID_{50}$/mL	20,000x
	A/Hong Kong/8/68	$1.00x10^5$ $TCID_{50}$/mL	20,000x
	A/Alice	$4.70x10^3$ $TCID_{50}$/mL	940x
	A/MRC 2	$8.17x10^3$ $TCID_{50}$/mL	1,634x
	A/Brisbane/10/07	$8.17x10^3$ $TCID_{50}$/mL	1,634x
Influenza B	**B/FL/04/06**	$1.67x10^4$ $TCID_{50}$/mL	278x
	B/Lee/40	$8.17x10^3$ $TCID_{50}$/mL	136x
	B/Taiwan/2/62	$5.03x10^4$ $TCID_{50}$/mL	838x
	B/GL/1739/54	$8.17x10^3$ $TCID_{50}$/mL	136x
	B/Maryland/1/59	$8.17x10^3$ $TCID_{50}$/mL	136x
	B/Florida/07/04	$1.00x10^5$ $TCID_{50}$/mL	1,667x
	B/Malaysia/2506/04	$5.67x10^3$ $TCID_{50}$/mL	95x

Virus or Bacterium	Type / Strain	Test Concentration	Multiple of LoD
	B/Allen/45	$1.00x10^5$ $TCID_{50}$/mL	1,667x
	B/HongKong/5/72	$8.17x10^3$ $TCID_{50}$/mL	136x
	B/Brigit	$3.50x10^4$ $TCID_{50}$/mL	583x
Parainfluenza Virus	**Type 1** Zeptometrix # 0810014CF	$1.39x10^4$ $TCID_{50}$/mL	28x
	Type 2 Zeptometrix # 0810015CF	$1.67x10^4$ $TCID_{50}$/mL	1,670x
	Type 3 Zeptometrix # 0810016CF	$1.00x10^5$ $TCID_{50}$/mL	10,000x
	Type 4 Zeptometrix #0810060CF	$5.67x10^3$ $TCID_{50}$/mL[a]	1.13x[a]
Respiratory Syncytial Virus	**A**	$1.39x10^4$ $TCID_{50}$/mL	6,950x
	B	$2.14x10^4$ $TCID_{50}$/mL	10,700x
Bordetella pertussis	E431	$1.00x10^6$ CFU/mL	250x
	A639		
	ATCC 8467		
	ATCC 9797		
	ATCC 51445		
	ATCC BAA-589		
	ATCC 9340		
	ATCC 10380		
	ATCC BAA-1335		
Chlamydophila pneumoniae	TW183	$2.42x10^5$ copies/mL	81x
Mycoplasma pneumoniae	M129	$1.88x10^5$ $TCID_{50}$/mL	6,267x
	ATCC 15531	$4.27x10^5$ CFU/mL	n/a
	ATCC 15293	$1.00x10^6$ CCU/mL[b]	33,333x
	ATCC 15377		
	ATCC 15492		
	ATCC 29085		
	ATCC 29342		
	ATCC 39505		
	ATCC 49894		

[a] Highest test concentration possible based on the concentration of virus in the stock culture fluid.

[b] CCU = Color Changing Unit. Both $TCID_{50}$ and CCU were determined according to the Reed-Muench method. Quantification in CCU/mL was considered equivalent to quantification in $TCID_{50}$/mL.

The potential for the FilmArray RP system to cross-react with non-FilmArray RP organisms was evaluated by testing an exclusivity panel consisting of 25 bacteria, 8 viruses, and 1 fungus. These organisms were selected based on their relatedness to FilmArray RP analytes, clinical relevance (cause respiratory symptoms or represent nasopharyngeal flora), or high prevalence within the population (e.g. Herpes Simplex Virus). Negative sample matrix was spiked with bacteria or fungi at a concentration of 10^6 CFU/mL and viruses at a concentration between 10^4 - 10^5 $TCID_{50}$/mL, or the highest concentration possible. The

FilmArray RP system did not cross-react with the exclusivity panel organisms listed in Table 13.

Table 13. Non-FilmArray RP Exclusivity Panel

Bacteria	Strain / Isolate
Bordetella bronchiseptica	clinical isolate
Bordetella holmesii	F061
Chlamydia trachomatis	D-UW3
Corynebacterium diptheriae	ATCC14779
Escherichia coli	O157:H7
Haemophilus influenzae	MinnA
Lactobacillus acidophilus	Type strain
Lactobacillus plantarum	17-5
Legionella longbeacheae	Long Beach 4
Legionella micdadei	Tatlock
Legionella pneumophilia	Philadelphia
Moraxella catarrhalis	Ne 11 (type strain)
Mycobacterium tuberculosis	H37Ra-1
Mycoplasma hominis	ATCC 23114
Mycoplasma genitalium	ATCC 33530
Neisseria elongata	type strain
Neisseria gonorrhoeae	ATCC 700825
Neisseria meningitidis	M1027 (type strain)
Pseudomonas aeruginosa	Zeptometrix #0801519
Staphylococcus aureus	COL
Staphylococcus epidermidis	RP62A
Streptococcus pneumoniae	type 59
Streptococcus pyogenes	Zeptometrix #0801512
Streptococcus salivarius	ATCC 13419
Ureaplasma urealyticum	ATCC 27618

Viruses	Strain / Isolate
Bocavirus	Type 1 - Clinical specimen
Coronavirus SARS	Zeptometrix –Nucleic Acid
Cytomegalovirus (CMV)	AD-169 (VR-538)
Epstein-Barr Virus (EBV)	B95-8
Herpes Simplex Virus	Type 1
Measles Virus	Edmonston
Measles Virus	Zeptometrix # 0810025CF[a]
Mumps	Zeptometrix # 0810079CF
Fungi	**Strain / Isolate**
Candida albicans	Zeptometrix #0801504

[a]This viral stock produced one false positive Adenovirus result. The false positive was confirmed to be caused by Adenovirus contamination of the viral stock and was not due to cross-reactivity between the Adenovirus assay and Measles virus.

Precision (Reproducibility and Repeatability)

A multicenter reproducibility study was performed to determine between-site and overall reproducibility of the FilmArray RP system. Reproducibility testing occurred at three test sites utilizing a panel of twelve simulated NPS specimens spiked with various combinations

of respiratory pathogens (analytes) at three different test levels (high negative (LoD/10), low positive (1X LoD), and medium positive (3X LoD)). On each testing day, two operators at each site tested two aliquots of specimens on two different FilmArray instruments (six specimens per operator per instrument per day). Every specimen was tested four times a day on five days at the three testing sites, for a total of 60 tests per analyte per concentration. A total of 26 lots of reagents and 20 FilmArray instruments were utilized in the reproducibility study.

Repeatability testing included an additional 7 days of testing per analyte and concentration at one site, for a total of 12 days of testing.

Reproducibility and Repeatability study results for CoV OC43, CoV 229E, *B. pertussis*, *C. pneumoniae*, and *M. pneumoniae* are summarized in Tables 14-19.

Table 14. Summary of Positive Agreement, Negative Agreement, and Tm Results from Reproducibility Testing of Coronavirus OC43

Coronavirus OC43 ATCC VR-759		# Positive	# Negative	% Agreement with Expected Result [a]	95% CI	Mean Tm	%CV Tm	Observed Tm Range
Medium Positive (3X LoD) 1,800 $TCID_{50}$/mL	Site A	20/20	0/20	100%	83.2% – 100%	80.98	0.23	80.53 - 81.36
	Site B	20/20	0/20	100%	83.2% – 100%	81.39	0.25	81.04 - 81.82
	Site C	20/20	0/20	100%	83.2% – 100%	81.20	0.26	80.60 - 81.55
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**81.17**	**0.32**	**80.53 - 81.82**
Low Positive (1X LoD) 600 $TCID_{50}$/mL	Site A	20/20	0/20	100%	83.2% – 100%	80.82	0.26	80.29 - 81.25
	Site B	20/20	0/20	100%	83.2% – 100%	81.31	0.24	80.95 - 81.85
	Site C	20/20	0/20	100%	83.2% – 100%	81.07	0.37	80.40 - 81.58
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**81.07**	**0.38**	**80.29 - 81.85**
High Negative [b] (LoD/10) 60 $TCID_{50}$/mL	Site A	18/20	2/20	90.0%	68.3% - 98.8%	80.86	0.24	80.49 - 81.25
	Site B	14/20	6/20	70.0%	45.7% - 88.1%	81.29	0.28	80.92 - 81.81
	Site C	16/20	4/20	80.0%	56.3% - 94.3%	81.04	0.32	80.11 - 81.45
	All Sites	**48/60**	**12/60**	**80.0%**	**67.7% - 89.2%**	**81.07**	**0.36**	**80.11 - 81.81**
Negative	Site A	0/180	180/180	100%	98.0% - 100%			
	Site B	0/180	180/180	100%	98.0% - 100%			
	Site C	1/180	179/180	99.4%	96.9% - 100%			
	All Sites	**1/540**	**539/540**	**99.8%**	**99.0% - 100%**			

[a] Expected results for the "Medium Positive", the "Low Positive", and the "High Negative" panel members are positive. Expected result for the "Negative" panel member is negative.
[b] "High Negative" samples are targeted to be positive 20-80% of the time.

Table 15. Summary of Positive Agreement, Negative Agreement, and Tm Results from Reproducibility Testing of Coronavirus 229E

Coronavirus 229E ATCC VR-740		# Positive	# Negative	% Agreement with Expected Result[a]	95% CI	Mean Tm	%CV Tm	Observed Tm Range
Medium Positive (3X LoD) 12 $TCID_{50}$/mL	Site A	20/20	0/20	100%	83.2% – 100%	81.20	0.20	80.81 - 81.47
	Site B	20/20	0/20	100%	83.2% – 100%	81.80	0.32	81.35 - 82.18
	Site C	20/20	0/20	100%	83.2% – 100%	81.35	0.34	81.03 - 82.13
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**81.37**	**0.40**	**80.81 - 82.18**
Low Positive (1X LoD) 4 $TCID_{50}$/mL	Site A	20/20	0/20	100%	83.2% – 100%	81.19	0.21	80.83 - 81.66
	Site B	20/20	0/20	100%	83.2% – 100%	81.62	0.25	81.12 - 82.08
	Site C	20/20	0/20	100%	83.2% – 100%	81.09	0.32	80.30 - 81.56
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**81.31**	**0.38**	**80.30 - 82.08**
High Negative[b] (LoD/10) 0.4 $TCID_{50}$/mL	Site A	14/20	6/20	70%	45.7% - 88.1%	81.06	0.22	80.72 - 81.43
	Site B	7/20	13/20	35%	15.4% - 59.2%	81.54	0.24	81.15 - 82.08
	Site C	11/20	9/20	55%	31.5% - 76.9%	81.17	0.24	80.70 - 81.68
	All Sites	**32/60**	**28/60**	**53.3%**	**40.0% - 66.3%**	**81.25**	**0.34**	**80.70 - 82.08**
Negative	Site A	0/180	180/180	100%	98.0% - 100%			
	Site B	0/180	180/180	100%	98.0% - 100%			
	Site C	0/180	180/180	100%	98.0% - 100%			
	All Sites	**0/540**	**540/540**	**100%**	**99.3% – 100%**			

[a] Expected results for the "Medium Positive", the "Low Positive", and the "High Negative" panel members are positive. Expected result for the "Negative" panel member is negative.
[b] "High Negative" samples are targeted to be positive 20-80% of the time.

Table 16. Summary of Positive Agreement, Negative Agreement, and Tm Results from Reproducibility Testing of *Bordetella pertussis*

Bordetella pertussis A639		# Positive	# Negative	% Agreement with Expected Result[a]	95% CI	Mean Tm	%CV Tm	Observed Tm Range
Medium Positive (3X LoD) 12,000 CFU/mL	Site A	20/20	0/20	100%	83.2% – 100%	88.36	0.36	87.46 - 89.05
	Site B	20/20	0/20	100%	83.2% – 100%	88.81	0.29	88.26 - 89.20
	Site C	20/20	0/20	100%	83.2% – 100%	88.34	0.18	87.97 - 88.58
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**88.50**	**0.38**	**87.46 - 89.20**
Low Positive (1X LoD) 4,000 CFU/mL	Site A	20/20	0/20	100%	83.2% – 100%	88.39	0.28	87.73 - 88.96
	Site B	20/20	0/20	100%	83.2% – 100%	88.64	0.31	88.07 - 89.20
	Site C	20/20	0/20	100%	83.2% – 100%	88.22	0.28	87.74 - 88.67
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**88.42**	**0.34**	**87.73 - 89.20**
High Negative[b] (LoD/10) 400 CFU/mL	Site A	16/20	4/20	80.0%	56.3% - 94.3%	88.41	0.34	87.86 - 89.36
	Site B	12/20	8/20	60.0%	36.1% - 80.9%	88.70	0.32	88.33 - 89.29
	Site C	12/20	8/20	60.0%	36.1% - 80.9%	88.26	0.28	87.52 - 88.71
	All Sites	**40/60**	**20/60**	**66.7%**	**53.3% - 78.3%**	**88.46**	**0.37**	**87.52 - 89.36**
Negative	Site A	0/180	180/180	100%	98.0% - 100%			
	Site B	0/180	180/180	100%	98.0% - 100%			
	Site C	0/180	180/180	100%	98.0% - 100%			
	All Sites	**0/540**	**540/540**	**100%**	**99.3% – 100%**			

[a] Expected results for the "Medium Positive", the "Low Positive", and the "High Negative" panel members are positive. Expected result for the "Negative" panel member is negative.
[b] "High Negative" samples are targeted to be positive 20-80% of the time.

Table 17. Summary of Positive Agreement, Negative Agreement, and Tm Results from Reproducibility Testing of *Chlamydophila pneumoniae*

Chlamydophila pneumoniae TW183		# Positive	# Negative	% Agreement with Expected Result[a]	95% CI	Mean Tm	%CV Tm	Observed Tm Range
Medium Positive (3X LoD) 9,000 copies/mL	Site A	20/20	0/20	100%	83.2% – 100%	79.65	0.29	78.94 - 79.99
	Site B	20/20	0/20	100%	83.2% – 100%	80.27	0.30	79.88 - 80.82
	Site C	20/20	0/20	100%	83.2% – 100%	79.73	0.23	79.42 - 80.09
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**79.92**	**0.45**	**78.94 - 80.82**
Low Positive (1X LoD)	Site A	20/20	0/20	100%	83.2% – 100%	79.63	0.27	79.03 - 80.09
	Site B	19/20	1/20	95.0%	75.1% - 99.9%	80.15	0.28	79.68 - 80.62

3,000 copies/mL	Site C	20/20	0/20	100%	83.2% – 100%	79.61	0.30	78.84 - 80.09
	All Sites	**59/60**	**1/60**	**98.3%**	**91.1% - 100%**	**79.79**	**0.42**	**78.84 - 80.62**
High Negative[b] (LoD/10) 300 copies/mL	Site A	11/20	9/20	55.0%	31.5% - 76.9%	79.55	0.25	79.25 - 80.08
	Site B	14/20	6/20	70.0%	45.7% - 88.1%	80.02	0.29	79.66 - 80.72
	Site C	10/20	10/20	50.0%	27.2% - 72.8%	79.61	0.29	79.16 - 80.21
	All Sites	**35/60**	**25/60**	**58.3%**	**44.9% - 70.9%**	**79.72**	**0.38**	**79.16 - 80.72**
Negative	Site A	0/180	180/180	100%	98.0% - 100%			
	Site B	0/180	180/180	100%	98.0% - 100%			
	Site C	0/180	180/180	100%	98.0% - 100%			
	All Sites	**0/540**	**540/540**	**100%**	**99.3% – 100%**			

[a] Expected results for the "Medium Positive", the "Low Positive", and the "High Negative" panel members are positive. Expected result for the "Negative" panel member is negative.
[b] "High Negative" samples are targeted to be positive 20-80% of the time.

Table 18. Summary of Positive Agreement, Negative Agreement, and Tm Results from Reproducibility Testing of *Mycoplasma pneumoniae*

Mycoplasma pneumoniae Type 1 - M129		# Positive	# Negative	% Agreement with Expected Result[a]	95% CI	Mean Tm	%CV Tm	Observed Tm Range
Medium Positive (3X LoD) 90 $TCID_{50}$/mL	Site A	20/20	0/20	100%	83.2% – 100%	77.42	0.29	77.04 - 77.71
	Site B	20/20	0/20	100%	83.2% – 100%	77.94	0.33	77.59 - 78.30
	Site C	20/20	0/20	100%	83.2% – 100%	77.83	0.28	77.44 - 78.12
	All Sites	**60/60**	**0/60**	**100%**	**94.0% - 100%**	**77.75**	**0.38**	**77.04 - 78.30**
Low Positive (1X LoD) 30 $TCID_{50}$/mL	Site A	19/20	1/20	95.0%	75.1% - 99.9%	77.55	0.30	77.05 - 78.00
	Site B	17/20	3/20	85.0%	62.1% - 96.8%	77.96	0.33	77.36 - 78.37
	Site C	20/20	0/20	100%	83.2% – 100%	77.68	0.39	76.65 - 78.10
	All Sites	**56/60**	**4/60**	**93.3%**	**83.8% - 98.2%**	**77.73**	**0.40**	**76.65 - 78.37**
High Negative[b] (LoD/10) 3 $TCID_{50}$/mL	Site A	5/20	15/20	25.0%	8.7% - 49.1%	77.58	0.31	76.72 - 78.01
	Site B	4/20	16/20	20.0%	5.7% - 43.7%	78.01	0.27	77.67 - 78.45
	Site C	11/20	9/20	55.0%	31.5% - 76.9%	77.76	0.34	77.04 - 78.09
	All Sites	**20/60**	**40/60**	**33.3%**	**21.7% - 46.7%**	**77.78**	**0.38**	**76.72 - 78.45**
Negative	Site A	0/180	180/180	100%	98.0% - 100%			
	Site B	0/180	180/180	100%	98.0% - 100%			
	Site C	0/180	180/180	100%	98.0% - 100%			
	All Sites	**0/540**	**540/540**	**100%**	**99.3% – 100%**			

[a] Expected results for the "Medium Positive", the "Low Positive", and the "High Negative" panel members are positive. Expected result for the "Negative" panel member is negative.

[b] "High negative" samples are targeted to be positive 20-80% of the time.

Table 19. Summary of Positive Agreement Results for Repeatability Testing of Coronavirus OC43, Coronavirus 229E, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*

Spiked Organism	Moderate Positive (3x LoD)		Low Positive (1x LoD)		High Negative (0.1x LoD)	
	# Positive / Total	% Positive Results	# Positive / Total	% Positive Results	# Positive / Total	% Positive Results
Coronavirus OC43	48/48	100%	47/48	97.9%	33/48	68.8%
Coronavirus 229E	48/48	100%	48/48	100%	19/48	39.6%
Bordetella pertussis	48/48	100%	48/48	100%	27/48	56.3%
Chlamydophila pneumoniae	48/48	100%	46/48	95.8%	18/48	37.5%
Mycoplasma pneumoniae	48/48	100%	47/48	97.9%	19/48	39.6%

Interference

Substances that could be present in NPS samples or introduced during sample handling were evaluated for their potential to interfere with assay performance. Four different organism mixes containing FilmArray RP analytes were spiked into a simulated NPS (sNPS) sample matrix (human epithelial cells in VTM) at 5 x their respective LoDs. The 5x LoD organism concentration was chosen to be near the analyte LoD but also to provide consistent results for sample-to-sample comparison. Each FilmArray RP analyte was tested in the presence of each potentially interfering substance listed in Table 20. None of the substances tested were found to compete or interfere with the control or analyte assays in the FilmArray RP. The appropriate FilmArray RP assays do react with the Influenza A H1, Influenza A H3, and Influenza B viral material contained in the FluMist® vaccine.

Table 20. List of Potentially Interfering Substances Evaluated

Endogenous Substances	Competitive / Interfering Microorganisms	
Human Blood (with Na Citrate) (1% v/v)	Respiratory Syncytial Virus A	2.8 x 10^4 $TCID_{50}$/mL
Mucin (bovine submaxillary gland) (1% v/v)	Human Rhinovirus	1.1 x 10^4 $TCID_{50}$/mL
Human Genomic DNA: 0.2 ng/µL	Influenza A 2009 H1N1	1.0 x 10^5 $TCID_{50}$/mL
2 ng/µL	*Staphylococcus aureus*	1.0 x 10^6 CFU/mL
20 ng/µL	*Neisseria meningitidis*	1.0 x 10^6 CFU/mL
	Corynebacterium diptheriae	1.0 x 10^6 CFU/mL
Exogenous Substances		
Saline Nasal Spray with Preservatives (1% v/v)	Analgesic ointment (1% w/v)	
Nasal Decongestant Spray (Oxymetazoline HCl) (1%v/v)	Petroleum Jelly (1% w/v)	
Tobramycin (0.6 mg/mL)	Smokeless Tobacco (1% w/v)	
Mupirocin (2% w/v)	FluMist® Nasal Influenza Vaccine (2009-2010)	

Technique Specific Substances		
Laboratory Reagents:	**Viral Transport Media:**	**Swabs:**
Bleach (1%, 2%, 5% v/v)	Remel M4	Copan 168C (rayon / twisted aluminum shaft)
Disinfecting wipes	Remel M4-RT	Copan FloQ (flocked nylon / plastic shaft)
Ethanol (7% v/v)	Remel M5	Copan 175KS01 (polyester / aluminum shaft)
DNAzap (1% v/v)	Remel M6	Millipore 519CS01M (flocked nylon / plastic shaft)
RNaseOut (1% v/v)	Copan UTM	

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Idaho Technology Inc.
c/o Beth Lingenfelter
390 Wakara Way
Salt Lake City, UT 84108

MAY 15 2012

Re: K120267

Trade/Device Name:	FilmArray Respiratory Panel (RP)
Regulation Number:	21 CFR 866.3980
Regulation Name:	Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class:	Class II
Product Code:	OCC, OEM, OOU, OEP, OTG, NXD, OOI, OZZ, OZY, OZX
Dated:	April 3, 2012
Received:	April 5, 2012

Dear Ms. Lingenfelter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Uwe Scholf for

Sally A. Hojvat, M.Sc., Ph.D.
Director,
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: K120267

Device Name: FilmArray Respiratory Panel (RP)

FilmArray Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with the FilmArray instrument for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Rhinovirus/Enterovirus, Respiratory Syncytial Virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the Film Array RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Bordetella pertussis*, Coronavirus 229E, Coronavirus OC43, Influenza A/H1, Influenza A/H3, Influenza A/2009 H1, Influenza B, *Mycoplasma pneumoniae* Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for *Chlamydophila pneumoniae* were established primarily using contrived clinical specimens.

Due to the genetic similarity between human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

The FilmArray RP detects Adenovirus species C serotype 2 and serotype 6 with reduced sensitivity. It is recommended that specimens found to be negative for Adenovirus after examination using FilmArray RP be confirmed by an alternate method (e.g., FDA cleared molecular test or cell culture).

The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for influenza A were established when influenza A/2009 H1N1, A/H1, and A/H3 were the predominant influenza A viruses in circulation. Performance of detecting influenza A may vary if other influenza A strains are circulating or a novel influenza A virus emerges. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Prescription Use ___x____ (Part 21 CFR 801 Subpart D) AND/OR Over-the-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE—CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Tamara Fitzhugh

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K120267